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NEUROHUMORS: NOVEL AGENTS IN THE ACTION OF THE NERVOUS SYSTEM[1]

By Professor GEORGE HOWARD PARKER

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THE enunciation of the neurone theory by Waldeyer in 1891 was a fitting culmination of the neurological work of the nineteenth century. By means of it many detailed questions on the structure and the function of the nervous elements found satisfactory and final answers, but as a result of it there also arose a host of new and perplexing problems, many of which are still unsolved. Prominent among these is that concerning the relations of nerve-cells or neurones not only among themselves but also between them and the cells of receptor and effector organs.

Embryonic nerve-cells or neuroblasts are at the outset reasonably separate and independent entities without special functional interdependence. As they grow and differentiate they come to form systems of conducting pathways by which one remote part of the body is brought into nervous connection with another. How neurones are related in such conducting systems has been a matter of dispute. Some histologists have claimed that the processes of one neurone fuse with those of the next and thus establish possibilities of nervous conduction; others have declared that such processes are only in contact one with another. The importance of this question disappeared, however, when it was found that degenerative changes started in one neurone never pass over the assumed boundary into the next neurone and that nerve impulses, which may course in either direction up or down a neurone, are limited to one direction in passing from neurone to neurone. Thus, whether neurone tips are fused with each other or are merely in contact, their region of joining, the so-called synapse, must be a differentiated area polarized as to its direction of transmis-

[1] An address given at the annual meeting of the Worcester Chapter of the Sigma Xi, on November 5, 1934.

sion. Thus in a way the old and rather discredited "law of forward conduction" receives a certain restricted justification.

The capacity of the synapse to limit the direction of transmission has often been compared to the action of a valve. But this is obviously a figurative statement, for the nerve impulse is not a gush of fluid through a tube whose direction of transmission is controlled by valvular devices. What, may we ask, is it that passes over the synapse? Two possible answers to this question have been put very clearly by Gerard, who has stated that either the same kind of ion migration and chemical change which represents the impulse itself passes over the synapse from neurone to neurone or the terminals of the discharging neurone act as miniature glands and, when stimulated, produce some chemical which is able to excite the tips of the next neurone and thereby initiate another impulse. Since the first of these hypotheses offers no explanation for synaptic polarization, while the second does, modern opinion has drifted consistently toward the latter. This view implies a chemical interpretation of the interaction of nervous elements, a view which in a certain measure was long ago advocated for sense-cells and their conducting elements by Botezat. It is to be met with continually in the writings of the late Ramón-y-Cajal and has been suggested for central organs by Sir Charles Sherrington and his associates. The chemical substance produced in this assumed activity, whereby one neurone may excite a neighboring neurone or other appended cell, has been called a neurohumor, to use a term introduced some years ago by Henri Frederieq. Such substances include in my opinion not only materials like acetyl choline as recently discussed from this standpoint by Sir Henry Dale and his fellow workers and Cannon's sympathin, but also adrenalin and those products of the pituitary gland which are known to activate animal effectors.

Neurohumors may act over distances of microscopic if not ultramicroscopic proportions or over large ranges in the animal body. Such substances, irrespective of their extent of spread, are in principle nervous activators and their grouping under one head, namely, that of neurohumors, is fully justifiable. Some students of this subject would class all neurohumors as hormones; others would include under this heading only such as act over long distances, but this does not seem to me to be a matter of serious import. Neurohumors really act as hormones over shorter or longer ranges. The precise problem that we have to face is not the classification of neurohumors, but the extent to which these substances actually exist. To that question we may now address ourselves, and in approaching it I shall deal chiefly with the nervous control of the melanophores in fishes.

In 1876 Pouchet showed that if the integumentary nerves of a turbot are cut, the denervated area of skin thus produced becomes dark through the dispersion of the melanin granules contained within its melanophores. The nerve-fibers concerned in this operation were shown to be autonomic in origin. Their great abundance and button-like terminals were demonstrated in a number of fishes by Ballowitz in 1893. As a result of these discoveries the nervous control of melanophores in fishes was accepted by practically all workers in this field, a conclusion amply supported by the later exhaustive investigations of von Frisch. The neurohumoral interpretation of these results is to the effect that the nerve-terminals applied to the chromatophores do not excite these cells directly, as is generally believed, but that these endings secrete a neurohumor which on reaching the color-cells induces them to respond in an appropriate way. Is there any evidence that such neurohumors play a real part in the color changes of fishes? A test of this question has been attempted on the common killifish, *Fundulus heteroclitus,* which has well-marked dark and light phases.

If a small transverse cut about a millimeter in length is made through a single fin-ray near the root of the tail of a light Fundulus, small bundles of radial nerve-fibers going to a restricted part of the tail will be severed and the denervated area thus produced will become evident as a dark, radiating band extending from the cut to the posterior margin of the tail. Such a band will begin to appear in about half a minute after the cut has been made and will grow in intensity for a short time, after which it may remain visible for several days. Under the microscope the band can be seen to be made up of melanophores whose pigment is fully dispersed, a condition in strong contrast with that of the color-cells in the rest of the tail where the melanin is densely concentrated near the cell centers.

Such a dark denervated band will maintain itself for as much as several days, even though the fish on which it has been formed is kept in a white-walled, illuminated aquarium, a condition under which the light coloration of the fish as a whole is retained. Gradually, however, the band begins to blanch and sooner or later it disappears by taking on the light tint of the fish. Bands of this kind may be called primary bands.

If such a light fish with a completely or nearly completely blanched primary band is put in a black-walled, illuminated aquarium, the fish, with the exception of the band, turns dark in less than two hours. The band, though denervated, then also darkens but only gradually and finally in a little less than a day it becomes as dark as the rest of the fish. The converse

change follows a corresponding course. When a dark fish with a denervated band in its tail is put into a white-walled aquarium, the fish as a whole blanches in rather less than five hours and the band in a little over a day. Bands either light or dark that are produced after the initial or primary band has disappeared may be called secondary bands and such bands change with the changes in the surroundings as the body of the fish does but with a very considerable lag.

When the fading of a primary band is followed in detail, it is seen that the band does not blanch uniformly and as a whole, but it begins to disappear first on its edges, as pointed out several years ago by Mills, and this process gradually spreads towards its axis, which is the last part to fade. The disappearance and reappearance of secondary bands also take place by lateral disintegration. According to the neurohumoral hypothesis, this process is to be understood as a response on the part of the denervated band to materials produced in the adjacent innervated portion of the tail. These materials make their way gradually from the regions of their origin into the band and thus effect a change in the melanophores there corresponding to that seen in the innervated area. In fact, it seems to me very difficult to explain these changes in any other way. It is well known, for instance, that these changes can have nothing to do with the possible degeneration or regeneration of the local nerve-fibers, for it has been shown that these fibers do not degenerate till some twelve days after they have been cut and that they regenerate in only about twenty to twenty-five days after this operation. The disappearance and reappearance of the bands, as already described, may be excited any time after the blanching of the primary band, that is, after two or three days following the exciting cut. That the nerve-fibers in a blanched primary band are still fully active can be shown by recutting such a band in a region slightly distal to the initial cut. By this means the band may be fully revived from the new cut to the free edge of the tail, showing that in its blanched condition the nerves in the band have gone into a temporarily quiescent state and are in no sense degenerated.

The primary band is apparently due to nerve impulses which for a time after the initiating cut has been made emanate from that region and excite the more distally located melanophores to disperse their pigment. If such an assumption is correct, it ought to be possible by an appropriate block to intercept such impulses and thereby obliterate the band. The most appropriate means of doing this is cold. If a capillary glass tube carrying dilute alcohol chilled to a degree well below 0° C. is applied to a fairly mature primary band, the distal part of the band that is separated from the cut by the tube soon blanches. This response justified the view that the band is dependent upon a flow of impulses from the region of the initiating cut.

How these impulses are produced is not easily stated. Since in the normal locomotion of the fish the tail is more or less continuously moved from side to side, it might be supposed that the friction thus generated in the cut would be the means of exciting impulses. If, however, in place of the usual small transverse incision in the tail, a square window is cut therein whereby the cut faces of the wound are no longer capable of rubbing one against the other, the band will nevertheless appear. It must, therefore, be admitted that the nerve impulses that call forth the band are not the simple result of the rubbing of the faces of the wound. How these impulses originate can not be stated. Probably they are dependent upon some more subtle form of stimulation in the cut, for it seems clear that the primary band is due to a flow of impulses from the cut region to the more distal melanophores. With the subsidence of this excitation the primary band gradually disappears, a step much in advance of the degeneration of the nerve-fibers in the region concerned.

After the disappearance of the primary dark band the revival of bands which resemble but lag behind the bodily color-changes have been ascribed to neurohumors and presumably to two sets of these substances one exciting a concentration of melanin in the containing cells and the other its dispersion. This interpretation suggests double innervation for these cells, a belief that is substantiated by the fact that when the exact areas of a given dark band and of its light equivalent are accurately compared, they are found not to agree precisely (Mills). This state of affairs is difficult to understand, except on the assumption of a double set of nerve-fibers, one for pigment concentration and the other for its dispersion.

If two sets of nerve-fibers are present for the melanophores in Fundulus, two sets of neurohumors are to be expected. Evidence in favor of the duplicity of these agents is afforded by experiments with flanking dark bands. Such experiments are best seen in the tails of the catfish Ameiurus, though they can be demonstrated in the tails of other fishes such as Fundulus. If two short, initial, dark bands are produced in the tail of a light catfish and in such positions that an intervening band of innervated tissue is left between them, the flanking bands of course darken; the area between them, however, remains light. If now the same test is tried but with a difference that the intervening band is a denervated blanched one and the dark flanking bands are short ones and of such a length as to abut only the distal half of the blanched

band, this band in a short time shows a remarkable state. Its proximal half, that which adjoins the light area of the tail, remains light, while its distal half, flanked by the newly formed dark bands, becomes conspicuously dark. From these experiments two conclusions can be drawn: first, that from the dark flanking bands something makes its way into the denervated light band and darkens it, a dispersing neurohumor; and, second, that an innervated light band can resist this darkening by something produced by its nerve-fibers, a concentrating neurohumor. It seems highly probable, therefore, that there are not only concentrating and dispersing nerve-fibers but also corresponding neurohumors.

The spread of these neurohumors over the millimeter or two of integument which may constitute the width of a band is from the side of the band inward toward its axis. This spread takes place at a very slow rate, the whole operation often requiring as much as a day. This slow axial spread makes it very improbable that the transfer of the neurohumors is by means of the blood and lymph of the given region. That blood and lymph are not concerned in this operation is shown in at least two ways. If adrenalin is injected into a Fundulus with a dark caudal band, this band disappears within less than a quarter of an hour and disappears as a whole, not by disintegration from the sides. This type of disappearance is what would be expected from a neurohumor carried in the blood, for the whole undersurface of the band is open to approach from the circulatory system. Further, as Matthews has recently shown, the blood from a dark Fundulus does not produce a dark spot when injected into a light Fundulus and *vice versa*. From these two standpoints it, therefore, seems clear that if neurohumors are produced by the melanophore nerves in Fundulus, these are not transmitted to the color-cells by the blood. They are probably not water-soluble. That they do make their way across the millimeter or more of denervated skin in the band can not be doubted. Hence it is concluded that they must be carried by some other solvent than water. I have expressed the opinion that they are soluble in oil and that they are transmitted from cell to cell by the fatty or lipoid constituents of these bodies. Such a means of transmission is quite consistent with the facts that have been learned concerning the appearance and disappearance of caudal bands, particularly the lateral decay of these bands and their notable lag behind the color changes of the fish as a whole.

A conclusion such as that just arrived at naturally raises the question of evidence for or against oil-soluble neurohumors. An attempt to ascertain whether there are such neurohumors has been made on the common dogfish, *Mustelus canis*. This fish, like Fundulus, has two well-marked color phases, one dark and the other light. As might be expected, the dark phase results from the dispersion of melanin in the dermal melanophores and the light one from its concentration. As Lundstrom and Bard showed in 1932, when the pituitary gland of a dogfish is removed, the fish becomes permanently light-tinted. On injecting a water extract of the gland into such a light fish the dark phase is temporarily reassumed. Moreover, the injection of defibrinated blood from a dark fish into a light one produces a temporary dark spot about the region of injection. These facts led Lundstrom and Bard to conclude that the dark phase of Mustelus is due to a substance produced in the pituitary gland and carried from that gland in the blood of the animal to its dermal melanophores.

Two years later Parker and Porter showed that when the integumentary nerves of a dogfish are cut, the denervated area thus produced becomes very light, even lighter in tint than that of the ordinary light dogfish. It, therefore, appears that in the dogfish, although the dark phase is produced by a dispersing neurohumor carried in the blood, the light phase is a nerve response of strictly local occurrence. The question naturally arises, Is there a neurohumor associated with this light phase? As has already been indicated, when the defibrinated blood of a light dogfish is injected into a dark one, no color change can be detected. Hence if the light phase is induced by a neurohumor, the neurohumor involved, since it is not carried in the blood, is probably not soluble in water. Is it soluble in oil? To test this question the fins of a light dogfish, the most responsive parts of its body, were reduced to a pulp by grinding them in a pulping machine. This pulp was then extracted with pure Italian olive oil. The oily residue thus obtained was injected with proper precautions into a dark dogfish, which in course of time showed a striking light spot near the region of injection. Under the microscope the melanophore pigment in this spot was seen to be concentrated in the color-cells, a condition that could be temporarily overcome by the injection of pituitrin into the animal. Light spots of the kind described did not result from simple oil injections. An ether extract of the fins also induced the formation of light spots in the fish. Extracts from fresh fins or from fins that had been dried for over a day at 110° C. were equally effective. These observations support the conclusion that in Mustelus beside the water-soluble pituitary neurohumor by which the melanophores are induced to disperse their melanin and thereby darken the fish, there is also an oil-soluble neurohumor that is equally effective in bringing about pigment concentration. This at least seems reasonable in view of what has already been described for the

concentrating neurohumor of Fundulus. These studies on the so-called nervous control of the melanophores of fishes point with great certainty to neurohumors as the agents really concerned and suggest the probability that there are two classes of such agents, one of which consists of materials, like pituitrin, soluble in water and hence transportable by the blood, hydroneurohumors, and the other soluble in oil and hence transmissible through the fatty or lipoid constituent of the tissues, liponeurohumors.

Although the instances here discussed are taken from only a single group of effectors, chromatophores, and their nervous connections, it is possible that reactions of this kind extend throughout the whole of the nervous organization of animals and that the relation of receptor cells to neurones, of one neurone to another, as well as of neurones to effectors, may be based upon the same principle that appears to apply to chromatophores. This in fact is the neurohumoral hypothesis, a view which in its essence has been expressed already by a number of workers and which under the general caption of the chemical interrelation of nervous elements has permeated the thinking of not a few of the neurologists of to-day.

THE UNSOLVED PROBLEMS OF LEPROSY[1]

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THE earliest medical records from Egypt and India are said to include descriptions of clinical leprosy.[2] Although the somewhat indeterminate description of cutaneous ills summarized in the term "zaraath" in the Old Testament may well have included several separate entities there is every reason to believe that it was incidentally descriptive of the disease now known as leprosy. The horror, fear and pity which leprosy in its exaggerated forms have always excited led to early attempts at segregation of its sufferers in many places. At all events the modern clinical description of leprosy dates from the work of Danielsenn and Boeck in 1847. It seems certain that Hansen in 1868, and even before he had anilin dyes to use, actually described with fidelity the massive aggregates or globi of the leprosy bacillus which we now recognize as a constant feature in the cutaneous form of the disease. In spite of these two relatively early evidences of objective certainty, the history of leprosy as a process remains in many of its significant phases as baffling to-day as it was a century ago. It may well take all the short time placed at my disposal to list with anything like sequential probability what the outstanding and unsolved problems of leprosy are, but this, at least, I shall attempt to do, with the further hope that I may emphasize two of the main junction points in the historical pathway which this brief survey covers.

It is still uncertain precisely what effect the segregation of lepers has had in suppressing the disease. Such isolation can never be completely carried out, particularly under the conditions of living in those countries where it is most prevalent, and a belief in its effectiveness is based largely on the disappearance of leprosy from Continental Europe in the Middle Ages, although certain other factors, such as other decimating epidemics, changes in dietary and even of climate, may well be involved. At all events the disease still remains in precisely those localities of the world where it was first described, in Africa, in the Orient and in the West Indies. Until we know more fully the precise epidemiology of leprosy no process of segregation could be expected to be efficient.

There is no question as to the great prevalence of leprosy in the early years of life, and the modern trend of thought goes farther in believing that infection takes place, at least in the majority of instances, in these very same early years, irrespective of the precise time of its clinical detection. We would not go so far as does Manaling, who, in view of the slow development of the disease and its frequent spontaneous cure in children before the complete evolution of the disease, would deny the possibility of its inception in adult life. In fact, there are recent well-controlled instances of accidental and experimental infection which render it probable that natural adult infection normally, although perhaps rarely, occurs.[3]

Far too little attempt, it would seem to us, has been made to ascertain the possibility of eliminating leprosy by immediate segregation at birth. Most of the references on the effect of removing the offspring of leper parents are misquoted and deal rather with separation at varying periods after birth than at the moment of delivery. The extraordinarily important results reported by Hasseltine in Honolulu have not, so far as we are able to determine from the literature, or on direct inquiry from those most concerned, been followed up. It will be recalled that Hasseltine found

[1] Address delivered before Section N—Medical Sciences, American Association for the Advancement of Science, Pittsburgh, December 31, 1934.

[2] Rogers and Muir.

[3] deLangen, Marchoux.

a single case of leprosy over a period of fifteen years in 219 children who had been removed from their leper parents at birth. In further investigation of these results, and in their prompt general application if they are confirmed, lies in our mind the first important pathway toward the eradication of the disease.

One of the most striking features of leprosy is its differentiation into types which may be so extreme as to justify a restricted diagnosis of the disease as "neural," "cutaneous" or finally "tuberculoid." All combinations of these extreme forms exist and they are all apparently preceded by the identical primary lesion. The several forms furthermore markedly predominate in certain countries; for example, although all types exist in the United States, on the other hand the cutaneous form is almost exclusively seen in the Philippines, and the neural form bulks large in India.

These clinical forms of the disease are extremely divergent in their individual pathology, and these differences are marked particularly by the almost complete absence from the neural form of the enormous numbers of acid-fast bacilli which are constantly present in the moderately advanced cutaneous disease. Diagnosis, indeed, in the neural form is often difficult, owing to the absence of the characteristic bacteria which facilitate recognition of the cutaneous form. One may well speculate as to this diversity of clinical types, which involves not only geographical distribution, conceivably owing to differences in climate, and which is also accompanied by marked differences in spontaneous cure, the neural form being on the whole milder and more frequently recoverable. This leads us directly to a consideration of the etiological agent of the disease itself.

We have already referred to the enormous aggregates of acid-fast bacteria that are found in typical cutaneous cases of leprosy, but non-acid-fast and even branching forms and forms like the Much granules in tuberculosis have also been casually observed. These latter forms might seem more significant if they were diligently sought for and it is not inconceivable that their relation to the neural form is an important one.

A series of observers since Neisser, nearly fifty years ago (1886), aggregating well over 60 authors or groups of authors to date and involving many more separate publications, are readily to be found in literature. Each of these authors in turn has believed that he alone has isolated the true organism of leprosy and feels that each of his predecessors has at best been only partially successful in attaining the desired result. A recent critical survey of this baffling question has led us to a belief somewhat different from the usual accepted one, namely, that a number of these observers have in reality grown the specific microorganism, rather than the generally accepted view that no one or only one particular investigator has as y been successful. We should be embarrassed to a tempt to name all these isolations which we shou regard as etiologically correct. One is inclined first glance to rule out the numerous observatio which impute etiological significance to Gram-positiv non-acid-fast diphtheroids if it were not for two ma lines of argument. It is true that such organisms a readily found in the normal skin. On the other han it is certain that acid-fast contaminants might al be present.

In at least 18 instances in the 68 separate descrip tions of isolated organisms that we have found an studied, diphtheroids have been described, and so of these by investigators whose previous work woul inspire technical confidence. Both chromogenic an non-chromogenic acid-fast organisms have been ob tained in 32 instances, and in view of the recent wor on chromogenic variants of the tubercle bacillus no clearly established, there is no inherent reason wh any of these isolations should not represent the tru etiological agent. We must confess here to an earl prejudice. Studies on organisms of the Actinomy cetales group by our regretted pupil, Edith Claypol showed in no uncertain fashion that in her unusua collection of pathogenic members of this genus, a studied over a period of years, individual pure strain not only varied from acid-fast bacilli to non-acid-fas Gram-positive organisms, but further to branchin non-acid-fast forms. Furthermore, all these varieti were observed in many single strains when studied a intervals over a long period; and cross immunity reactions were shown to occur between the divergen morphological forms. With this in mind we are recep tive to the claims of those 11 investigators who hav isolated what they have described as a "streptothrix" in cultures from leprosy as well as those 18 other who found diphtheroids. Some of these cultures were variably acid-fast and even branching. A few author have described both acid-fast bacilli, non-acid-fas diphtheroids and acid-fast streptothrix in successive isolations.

May we make our position perfectly clear in this matter by quoting a few specific references? We have personally no reasonable doubt that the non-chromogenic acid-fast bacillus isolated by Soule and McKinley, and which retains these characteristics, is the one that is present in characteristic fashion in cutaneous leprosy. But we feel also that it is quite likely that the diphtheroid isolated by Walker, at times, may represent another growth phase of the acid-fast organism which he also found. Salle's recent claim at transformation of a primary acid-fast isolation into a diphtheroid on subculture would,

if corroborated, prove this suggestion of various growth phases, which, to repeat, is not confined to the organism of leprosy.

The final and crucial proof of the correct etiological agent of leprosy still remains to be fulfilled. One spontaneous disease in animals, rat leprosy, apparently offers almost complete analogy to the human syndrome, including difficulty in culture of the microorganism in the lesion. In spite of this fact no one has, we believe, produced experimental leprosy in animals with material of human origin with anything like fidelity. No particular surprise need be occasioned by this failure. Many strictly human diseases have not been reproduced in animals, and some have succeeded only on the inoculation of anthropoid apes which have not been sufficiently tested in the case of leprosy. The time element would seem to us important in this connection. We know that human leprosy often requires years after the presumed, or, in a few instances, the known time of infection, before characteristic lesions with bacteria in them are found; so far as we know no experimental animals have been observed longer than a few weeks.

Another field for serious inquiry, in fact, the ultimately most important one in the study of leprosy, is that of specific therapy. There is a firm, and we believe an increasing conviction, that chaulmoogra oil derivatives are to a variable degree effective at least in ameliorating the symptoms and lesions of leprosy. The effectiveness so far depends not only on the preparation used but on the method of inoculation, and human trial must remain the ultimate criterion on which this or any other form of therapy is based. But it would seem as if a fairly obvious experimental method for the testing of the comparative value of anti-leprosy medicaments has only recently been tried; Anderson and his collaborators have compared several derivatives of chaulmoogra oil on rats spontaneously suffering from their own variety of leprosy and have been able to come to a certain decision in reference to the best of these preparations. Surely further attempts in this direction are indicated.

SCIENTIFIC EVENTS

THE FOURTH INTERNATIONAL CONGRESS OF AGRICULTURAL INDUSTRIES

THE fourth International Congress of Agricultural Industries, which is one of the many to be held in connection with the Brussels Universal Exposition of 1935, is being organized by the International Commission of Agricultural Industries.

It will be remembered that the third congress was held in March of last year, at Paris, and although intervals of three years between the congresses will ordinarily be observed, it was decided to hold the next one the following year in order to set up a more effective organization of the congresses and to take advantage of the Brussels exposition.

The congress will be organized in the four divisions: (1) General scientific studies; (2) Agronomic studies; (3) Industrial studies, and (4) Economic studies. There will be some twenty-six sections comprised in these four general divisions. In order to assure that subjects of timely interest are discussed, special reporters upon ten such topics will be appointed and the reports prepared by them printed and distributed in advance in order to assure fruitful discussion of these questions of "priority."

Communications are invited from all who may desire to take part in the program. The texts of communications in triplicate, together with brief abstracts, should be mailed before April 15. The membership fee is 100 French francs and for the families of members, 50 francs. Applications for membership and for further information should be addressed to the International Commission of Agricultural Industries, 156 Boulevard Magenta, Paris (X^e), France.

THE PAN AMERICAN INSTITUTE OF GEOGRAPHY AND HISTORY

A GEOGRAPHICAL and historical congress to organize an international bureau for the compilation of data on exploration was proposed by several South American countries as long ago as 1903. In 1928 at the sixth International Conference of American States plans were perfected for the organization of a Pan American Institute of Geography and History. Sr. Pedro C. Sanchez was appointed director of that institute, and in September, 1929, a meeting to conclude plans of organization was held in Mexico City. At that meeting Dr. Lawrence Martin, of the Division of Maps of the Library of Congress; Dr. George B. Winton, professor of history at Vanderbilt University, and Dr. William Bowie, chief of the Division of Geodesy, U. S. Coast and Geodetic Survey, represented this nation.

The first formal assembly of the institute was held at Rio de Janeiro in December, 1932. At that assembly the United States was represented by Hon. Edwin V. Morgan, Ambassador to Brazil, and Dr. Wallace W. Atwood, geographer, president of Clark University, Worcester, Massachusetts. At the final plenary session the City of Washington was selected as the place for the next meeting in 1935, and Dr. Atwood was chosen executive president for three years.

Several of those who are particularly interested in

the development of cultural relationships between the citizens of the United States and their Latin American neighbors to the south, have held informal conferences in Washington and made preliminary plans for the congress, which is to be held in Washington before the close of this year. Bills have been presented in both houses of the Congress in support of this enterprise. On February 19 Secretary of State Cordell Hull sent the following letter to the President of the United States:

Sir: The undersigned, the Secretary of State, has the honor to recommend that the Congress be requested to enact legislation providing for an annual appropriation of $10,000 for the payment of the share of this Government in the expenses of the Pan American Institute of Geography and History; to request the President to invite the Pan American Institute of Geography and History to hold its second general assembly in the United States in 1935, and to provide an appropriation of $10,000 for the expenses of such a meeting.

There is attached hereto a statement containing the history of the Pan American Institute of Geography and History.

Membership of the United States in the Institute would be desirable as the Institute will provide an international agency for the collection, coordination and dissemination of geographical and historical information which will be of value to numerous organs of the Government of the United States, scientific organizations, educational institutions and interested scholars.

This is the first organization of a Pan American character to be established in Mexico. The Mexican Government has made generous provision for the Institute including the erection of an appropriate and handsome building for its use. The next meeting of the assembly of the Institute is scheduled to take place in Washington in 1935. It is believed that Mexico as well as the other members of the Pan American Union would view with great gratification the support of the Institute by the United States.

On February 20 President Franklin D. Roosevelt sent the following message to Congress:

I commend to the favorable consideration of the Congress the enclosed report from the Secretary of State, with an accompanying paper, to the end that legislation may be enacted providing for an annual appropriation of $10,000 for the payment of the share of this Government in the expenses of the Pan American Institute of Geography and History and requesting the President to invite the Pan American Institute of Geography and History to hold its second general assembly in the United States in 1935, and providing an appropriation of $10,000 for the expenses of such a meeting.

If and when the Congress has taken the necessary action, the invitations will be sent out by the President, or through officers of the State Department, to the various nations that are cooperating in this enterprise and a group of official delegates will be selected to represent the United States at the coming meeting. Preliminary plans call for a series of programs of general interest, in which progress in research work in geography and history and plans for cooperation between the American people in the promotion of such research will be presented. We anticipate that a number of sectional meetings will be necessary, for the organization recognizes the fields of archeology, pre-Columbian history, the Colonial epoch, as well as topography, cartography, geodesy, geomorphology, human geography, historical geography, biologic and economic geography.

In addition to the formal meetings, at which papers may be presented, a number of excursions to places of special interest in or near Washington will be planned for the delegates. It is anticipated that there will be one or two social occasions associated with the congress.

WALLACE W. ATWOOD, *President,*
Pan American Institute of Geography and History

THE LANCASTER BRANCH OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

AT a meeting of the executive committee of the American Association for the Advancement of Science held in New York on October 21, a committee was appointed with special reference to the organization of local branches of the association, and the first branch under its auspices authorized by the council at the Pittsburgh meeting of the association has been established at Lancaster, Pa.

A preliminary organization meeting, with seventy of those interested in the movement in attendance, was held at Franklin and Marshall College in December. Jaques Cattell, vice-president of the Science Press Printing Company, after stating briefly the object of the meeting, introduced Dr. Otis W. Caldwell, professor of education and director of the Institute of School Experimentation at Teachers College, Columbia University, chairman of the committee on organization and now general secretary of the association. Dr. Caldwell gave an account of the work for the advancement and diffusion of science of the association and described how its objects could be promoted by the establishment of local branches. As the result of the discussion following Dr. Caldwell's address, which was led by Dr. Paul L. Whitely, professor of psychology at Franklin and Marshall College, acting as temporary chairman, a committee on organization was appointed.

The first regular meeting was held on February 13, at Franklin and Marshall College, at which Dr. W. F. G. Swann, director of the Bartol Research Foun-

dation of the Franklin Institute, was guest lecturer. He spoke on "Cosmic Rays Simplified" before an audience of approximately four hundred and fifty people. Following the lecture he gave a cello recital of six numbers accompanied by Dr. Barrows Dunham, assistant professor of English at Franklin and Marshall College. Before the lecture a dinner was given in honor of Dr. Swann, at which fourteen members especially interested in the success of the branch were present.

The following officers were elected: *Chairman,* Jaques Cattell; *Vice-chairman,* Dr. Clarence C. Vogt; *Treasurer,* Professor H. M. Fry; *Secretary,* Dr. Frances A. Coventry. Dr. Noel P. Laird was made chairman of the publicity committee. This committee is composed of representatives from the Hamilton Watch Company, the Lancaster City Schools, the Lancaster County Schools, the Millersville State Teachers College, the Armstrong Cork Company, the Lancaster Medical Societies, the Lancaster College Club, the Harris Dental Society, the Muhlenberg Botanical Society and other organizations.

One hundred and two members had joined the branch at the time of the meeting. Since then the membership has increased to almost four hundred. Dues have been set at $1 per year, and it is planned to hold meetings monthly from September to June.

The second meeting was scheduled for March 20 with William McAndrew, formerly superintendent of schools in Chicago, as the lecturer. The third meeting is planned for the second week in April, when the speakers will be M. and Mme. Jean Piccard.

F. A. COVENTRY,
Secretary

THE ENGINEERING INDEX

DR. FRANK B. JEWETT, president of Bell Telephone Laboratories and vice-president of the American Telephone and Telegraph Company, has accepted the position of national chairman of a campaign to raise a working capital fund of $161,000 for "Engineering Index, Inc." Announcement of Dr. Jewett's acceptance was made by Collins P. Bliss, president of the index and dean of the School of Engineering of New York University, who has headed a movement to save the fifty-year-old index and annotating service of the engineering profession since it was discontinued as an activity of the American Society of Mechanical Engineers a year ago. In accepting the chairmanship of the Engineering Index National Committee, Dr. Jewett said:

> Only my deep concern for the preservation of this essential service could induce me to accept this responsibility. The keeping of the records of science is one of the most important and valuable activities. To-day the index is the only agency which makes available to the engineer and research worker an exhaustive and continuing record of findings and developments in the technical field.
>
> In view of the enormous, unwieldy mass of current engineering literature, the absence of such a service would have serious and far-reaching consequences. Certainly if duplication of effort and the resulting economic loss is to be minimized, it is essential for the research worker at all times to be in a position to profit by what others have done and are doing.
>
> During the past year the continuance of *Engineering Index* as a non-profit corporation has been the concern of a small group of educators and engineers. The majority utilizing its service have taken such continuance for granted. It is my belief that if representative members of the profession and of industry are apprised of the actual situation, they will cooperate in providing funds needed to insure its permanence and make possible a program to widen its use.
>
> I join with Dean Bliss and the others on the National Committee, in the belief that preservation of *Engineering Index* is one of the most important jobs confronting the profession to-day. Soundly established, with adequate facilities for the exhaustive and systematic annotating and reporting of the findings in both pure and applied science, it will be insurance of continued and orderly progress, and as such, a national asset. Its support by industry is a matter of enlightened self-interest.

The National Committee is not as yet completely enrolled. It, however, already includes the names of a large number of those prominent in engineering and in industry.

RECENT DEATHS

DR. JOHN JAMES RICKARD MACLEOD, professor of physiology in the University of Aberdeen, died on March 16, at the age of fifty-eight years. Dr. Macleod, who received the Nobel prize with Sir Frederick Banting for their discovery of insulin, was professor of physiology at Western Reserve University from 1903 to 1918 and for the next ten years at Toronto.

DR. JOHN RUHRÄH, professor of the diseases of children at the University of Maryland, died on March 10 at the age of fifty-eight years.

DR. DANIEL COLQUHOUN, emeritus professor of medicine in the University of Otago, New Zealand, died on February 17.

Nature records the death of Professor Emanuele Paternò, formerly professor of general chemistry at the University of Rome, and of Dr. Axel Wallén, director of the State Meteorological Hydrographic Institute of Sweden.

SCIENTIFIC NOTES AND NEWS

THE annual stated meeting of the National Academy of Sciences will be held under the presidency of Dr. W. W. Campbell, in the building of the academy at Washington, on April 22, 23 and 24. The autumn meeting will be held at the University of Virginia on November 18, 19 and 20.

THE spring meeting of the Executive Committee of the American Association for the Advancement of Science will be held in New York City on April 14. Communications to be brought to the attention of the committee should be sent to the permanent secretary, the Smithsonian Institution Building, Washington, D. C.

DR. FREDERICK G. NOVY, retiring dean of the University of Michigan Medical School, at a special executive faculty meeting on February 7 was presented with a bronze plaque. The resolution inscribed on the plaque acknowledged Dr. Novy's years of service to the university and noted the regret of his colleagues that he will no longer be associated with them. Dr. Novy is succeeded as dean by Dr. Albert C. Furstenberg.

ON the occasion of his retirement on March 15 as Governor General and Commander-in-chief of New Zealand after five years of office, Lord Bledisloe presented to the Dominion a portrait of Lord Rutherford, a native of New Zealand, painted by Oswald Birley, also a New Zealander. The portrait will be hung in the new National Art Gallery at Wellington. Mr. Birley painted some three years ago a portrait of Lord Rutherford, which was presented to the Royal Institution and Lord Bledisloe commissioned him to paint the replica, which has now been sent to New Zealand.

IN honor of the eighty-eighth birthday on February 10 of Hofrat Dr. Gustav Riehl, emeritus professor of dermatology at the University of Vienna, the issues of the *Wiener klinische Wochenschrift* of February 8 and of the *Wiener medizinische Wochenschrift* of February 9 were dedicated to him.

THE annual award of the Pittsburgh Section of The American Chemical Society was on February 17 presented to Charles Edward Nesbit, chief chemist of the Edgar Thompson Steel Works and for many years the treasurer of the Pittsburgh Section. The title of the accompanying paper by Mr. Nesbit was "The Disintegration of Fire-Brick Linings in the Iron Blast Furnace."

THE Joseph A. Capps Prize for 1934 of the Institute of Medicine of Chicago has been awarded to Lars F. Gulbrandsen, instructor in bacteriology and public health at the University of Illinois College of Medicine, for his paper on "Invasion of the Body Tissues by Orally Ingested Bacteria and the Defensive Mechanism of the Gastro-Intestinal Tract." The prize of $500, established by an anonymous donor in honor of Dr. Joseph A. Capps, is awarded annually for the most meritorious medical research by a graduate of a medical school in Chicago completed within two years after graduation.

THE Osborne Reynolds Medal for meritorious contributions to the progress of the British Institution of Chemical Engineers has been awarded to H. J. Pooley, general secretary of the Society of Chemical Industry.

ROBERT J. MOORE, of the Bakelite Corporation, was reelected chairman for 1935–36 of the American Section of the Society of Chemical Industry at the meeting of the society held in New York City on March 8. Other officers elected for the ensuing year are: W. D. Turner, Columbia University, *vice-chairman;* Foster Dee Snell, Foster Dee Snell, Incorporated, *secretary;* J. W. H. Randall, consultant, *treasurer.* New members of the executive committee are: Wm. H. Gesell, Lehn and Fink, Incorporated; Elmer K. Bolton, E. I. du Pont de Nemours and Company; J. B. Rather, Socony-Vacuum Corporation; E. R. Weidlein, the Mellon Institute.

DR. JOHN F. BOVARD, dean and director of physical education at the University of Oregon and Oregon State College, has been elected president of the Northwest District of the American Physical Education Association.

DR. PETER O. OKKELBERG, professor of zoology in the University of Michigan, has been appointed to the newly created post of assistant dean of the graduate school. He will continue as secretary of the school, a position that he has filled during the past five years.

DR. RUDOLPH E. LANGER, professor of mathematics at the University of Wisconsin, has been appointed lecturer on mathematics and tutor in the division of mathematics at Harvard University.

DR. WILLIAM ORR SWAN, professor of chemistry at Southwestern, Memphis, Tenn., has been appointed head of the department of chemistry at the Virginia Military Institute. He succeeds Colonel Hunter Pendleton, who has served for the past forty-five years.

DR. I. R. POUNDER, assistant professor of mathematics at the University of Toronto, and Dr. A. H. S. Gillson, associate professor of mathematics at McGill University, have been promoted to full professorships.

DR. FREDERICK SEITZ, of Princeton University, has been appointed instructor in physics at the University

of Rochester, where he will have charge of the work in theoretical physics.

THE *Journal* of the American Medical Association reports that following the resignation of Kiheiji Onodera, president of the Tokyo Imperial University, the fifth presidential election took place on December 15. Professor Dr. Mataro Nagayo, dean of the medical department of the university, was elected the next president by the majority of 98 out of 164 votes. He was born in 1878 and had been director of the Infectious Disease Research Laboratory from 1919 to 1933. He was also president of the Cancer Research Institute. His present post of dean will be taken over by Professor Dr. Hisomi Nagai, professor of physiology in the university.

DR. NATHANIEL WALES FAXON, since 1922 director of the Strong Memorial Hospital of the University of Rochester, has been appointed director of the Massachusetts General Hospital and the Massachusetts Eye and Ear Infirmary, Boston. Dr. Faxon, who graduated from Harvard Medical School in 1905, was assistant director of the Massachusetts General Hospital from 1919 to 1922. He succeeds Dr. George H. Bigelow, who has been missing since December, 1934.

DR. ARTHUR D. LITTLE, who has retired as president of Arthur D. Little, Inc., has been elected chairman of the board. Dr. Little becomes chairman within a year of the fiftieth anniversary of the organization. His staff now includes graduates of twenty-two universities and technical schools.

SIR GEORGE NEWMAN will retire on March 31 from the posts of chief medical officer of the British Ministry of Health and of the Board of Education, and will be succeeded by Dr. A. Salusbury MacNalty, who, in turn, will be succeeded by Dr. Thomas Carnwath as deputy to the chief medical officer.

THE position of assistant entomologist at the Rothamsted Experimental Station, England, made vacant by the appointment of H. C. F. Newton as advisory entomologist to the West Midland Province, at the Harper Adams Agricultural College, Newport, has been filled by A. Coulston Evans, assistant plant pathologist at the Long Ashton Research Station of the University of Bristol.

THE Committee on Scientific Research of the American Medical Association has made a grant of $200 to Professor Israel S. Kleiner, of the New York Homeopathic Medical College and Flower Hospital, for work on the analysis of various materials for ascorbic acid (Vitamin C). The research work will be actively conducted by Dr. Henry Tauber.

THE Executive Committee of the Federation of American Societies for Experimental Biology announces the following awards of fellowships for attendance at the fifteenth International Physiological Congress, which will be held in Leningrad and Moscow next August. In physiology, Dr. J. M. Wolfe, Vanderbilt University; on biochemistry, Dr. Abraham White, Yale University; on pharmacology, Dr. Bernard M. Jacobson, Harvard Medical School, and in pathology, Dr. William Mahoney, Yale University.

DR. F. GREGORY HALL, professor of zoology at Duke University, has received a grant from the National Research Council to permit him to join an expedition that will leave in April for the Andes in northern Chile to study the physiological effects of extremely high altitudes on men and animals.

DR. NORBERT WIENER, professor of mathematics at the Massachusetts Institute of Technology, has been granted a leave of absence for the next academic year to join the faculty at the National Tsing Hua University at Peking, China.

DR. ARNOLD A. ZIMMERMANN, assistant professor of anatomy at the University of Illinois College of Medicine, Chicago, will continue his studies on the lymphatics of the opossum in the laboratories of the Wistar Institute of Anatomy, Philadelphia.

DR. JAMES JESSE TURNER, professor of biology at Hiram College, Ohio, has returned to the college after conducting an ecological study of the flora of the southeastern states, including the coastal plain and the swamps of Florida.

DR. HANS ZINSSER, of the Harvard Medical School, was the principal speaker at the annual dinner of the Columbia Alumni Club of Paris on February 12. Dr. Zinsser spoke of his work and in particular of the effect of disease on the political and military history of the world.

DR. DAVID P. BARR, professor of internal medicine in the School of Medicine of Washington University at St. Louis, recently returned from a trip to Australia, where he delivered a series of lectures at the special invitation of the Melbourne Permanent Post Graduate Association. This association conducts for the benefit of the physicians of the state of Victoria more or less continuous post graduate instruction. During the past decade it has been their custom to invite each second year a physician or surgeon either from England or from the United States to assist in this instruction and to give a series of stated lectures.

AT a meeting of the Electrochemical Society, held this week in New York City, Professor W. W. Stender, of the University of Leningrad, reported upon the new alkali-chlorine industry of Russia.

DR. C. A. EDWARDS, principal of University College, Swansea, Wales, gave a lecture at the museum of the Franklin Institute, Philadelphia, on March 8, entitled "A Consideration of the Internal Atomic Disturbances that Occur during the Straining of Metallic Crystals."

BARTRAM THOMAS, the English explorer and orientalist, lectured on his first crossing of the Great Southern Desert of Arabia before the University of Virginia on March 4.

PROFESSOR JOSEPH NEEDHAM, who is Sir William Dunne reader in biochemistry at the University of Cambridge, gave during March a series of three Terry lectures at Yale University. He spoke on the general topic of "Order and Life." The Terry lectures have been given in previous years by John Dewey, Robert A. Millikan, Arthur H. Compton, William E. Hocking and Henry Norris Russell.

THE fourth lecture in the Smith-Reed-Russell series at the School of Medicine of the George Washington University was given before the faculty and students on March 5 by Dr. E. V. McCollum, professor of biochemistry of the Johns Hopkins Medical School. Dr. McCollum's subject was "The Rôle of the Vitamins in Relation to the Bodily Resistance to the Infectious Diseases."

PROFESSOR HAROLD C. UREY, of Columbia University, gave a lecture on Monday, March 18, at the University of Rochester before a joint meeting of the Rochester Sections of the American Chemical Society and the Optical Society of America. His subject was "Isotopic Equilibria and Separation of Isotopes." Future meetings of the Rochester Section of the Optical Society are as follows: April 9, Dr. W. E. Forsythe, Cleveland, Ohio, "Light Sources for Photographic Purposes"; April 23, Professor Brian O'Brien, University of Rochester, "The National Geographic-United States Army Air Corps Stratosphere Flight"; May 14, Dr. Lyman J. Briggs, director, National Bureau of Standards, "The Work of the National Bureau of Standards."

THE New York Branch of the American Psychological Association will hold its sixth spring meeting at Princeton University, on Saturday, April 13, beginning at 9 o'clock. There will be sessions on comparative psychology, child and differential psychology, physiological psychology, experimental psychology and social and abnormal psychology; and an address by the honorary president, Dr. Joseph Jastrow.

THE one hundred and ninety-eighth regular meeting of the American Physical Society will be held in Washington, D. C., on April 25, 26 and 27. The Thursday and Friday sessions will be held at the Bureau of Standards and the Saturday sessions at the National Academy building. Other meetings during 1935 are as follows: June 21–22, Minneapolis; June 24–28, Los Angeles; November 29–30, Baltimore; December, the Pacific Coast; annual meeting, St. Louis, Mo.

THE first annual meeting of the American Institute of Tropical Medicine will open in New York City on Tuesday, April 16.

THE International Congress of Neurology will be held in London from July 29 to August 2.

DATES for the ninth season of the Allegany School of Natural History in Allegany State Park, New York, conducted by the Buffalo Society of Natural Sciences in cooperation with the New York State Museum and affiliated with the University of Buffalo, have been set for July 5 to August 24, 1935. Dr. Robert E. Coker, of Chapel Hill, N. C., is director of the school. The following courses will be given: in field botany by Dr. Robert B. Gordon, of the Ohio State University; in field geology by Gordon I. Atwater, of the University of Iowa; in the natural history of birds by Aretas A. Saunders, of the Central High School, Bridgeport, Conn.; in nature study, by Professor William P. Alexander, of the Buffalo Museum of Science; in field zoology, by Dr. Robert E. Coker. The administrative staff will include: Mrs. Robert E. Coker, dean of women; Esther W. Eno and Oscar M. Waddell, of the Buffalo Museum of Science, secretary and camp manager, respectively.

Nature reports a bequest from Lady Dewar, who died on January 7, of ten thousand pounds to the Royal Institution. The gift is free of duty, and is made on the condition that the income is to be used for the purpose of furthering scientific research in the institution and as a permanent memorial to the work there of her husband, Sir James Dewar, who succeeded Tyndall as superintendent of the institution in 1887. Lady Dewar has also left to the institution Sir James's medals and diplomas and his scientific papers and apparatus, together with a sum of money to provide accommodation for them. A large part of his apparatus, in particular that used in his low temperature researches, has remained at Albemarle Street since his death, and in recent years has been displayed in the institution's collection. The papers and objects now presented are additional material likely to be of historic value in relation to the period of Dewar's professorship. Lady Dewar's other bequests include £4,000 to the Royal Society's Mond Laboratory at Cambridge and £3,000 to the Royal Academy of Music. The residue of the estate is left for the furtherance of research in chemistry and physics at one of the Universities of Edinburgh, St. Andrews, Glasgow or

Aberdeen, or for the assistance of bacteriological research in connection with the Royal Infirmary of Edinburgh and the Glasgow Royal Infirmary.

IN recognition of the bequest of his valuable library of some 5,000 volumes to the Field Museum of Natural History, the late Dr. Berthold Laufer, formerly curator of anthropology at the museum, has been posthumously honored by election as a contributor of the institution. Contributors form a special class of membership designating those whose gifts in money or materials range in value from $1,000 to $100,000.

TWO new fellowships for graduate students in botany and chemistry for the coming year at the University of Oklahoma have been announced by Dr. Homer L. Dodge, dean of the graduate school. The Ray M. Balyeat fellowship, offering a $600 stipend for study in any school, will be given to encourage students to study chemical substances concerned with allergy. A fellowship and stipend, not yet determined, to encourage the study of wild plants of Oklahoma and their possibility as ornamentals, is being offered by Oklahoma garden clubs.

A NEW quarantine prohibiting movement of elm trees out of regulated areas in New York, New Jersey and Connecticut, because of the spread of the Dutch elm disease, took effect on February 25. The quarantine applies to all plants or parts of plants of all species of elms, whether grown in nurseries, forests or on private property. The campaign is under the direction of L. H. Worthley, of the Bureau of Entomology and Plant Quarantine, U. S. Department of Agriculture, with headquarters at White Plains, New York.

DISCUSSION

BALANCED DIETS, NET ENERGY VALUES AND SPECIFIC DYNAMIC EFFECTS

IN a recent number of SCIENCE[1] H. H. Mitchell presents a theoretical discussion of the subject of this communication, involving certain of the writer's published conclusions.

After developing a line of argument similar to and in harmony with that of the writer in the publication of the so-designated "law of maximum, normal nutritive value," Mitchell discusses the significance of this principle in relation to net energy values, saying, in part:

> With these definitions in mind, the first implication of the above-defined conception of nutritive balance in a ration or diet is that except for differences in digestibility, the net energy of all perfectly balanced rations is the same under the same conditions of feeding, or somewhat more precisely, the net availability of the metabolizable energy of all perfectly balanced rations is maximal for any imposed conditions of feeding.

Further, he says:

> However, Forbes' recently announced "law of maximum, normal nutritive value," although it advocates the use of completely balanced rations in determinations of net energy values, does not state nor imply that the net availability of the metabolizable energy of such rations will be maximal and identical.

It is true that, in my "law of maximum, normal nutritive value"[2] I avoided making any statement or implication to the effect that the net availability of the metabolizable energy of completely balanced rations is maximal and identical (though we had discussed the idea), because I can not conceive of balanced rations—as practicable entities—being so perfectly balanced that there would be no individuality of dynamic effect of the nutrients serving the same purposes in different rations, and that there would be no differences in either the excess nutrients, or in substances present without nutritive value, which would affect the economy of utilization of metabolizable energy.

One must remember, in theorizing, that in feeding practice we deal not with pure nutrients, of known identity and character, but—in each feeding stuff—with a vast complication of little-known substances.

Also, it is only fair to call attention to Mitchell's misstatement to the effect that my law of maximum, normal nutritive value "advocates the use of completely balanced rations in the determination of net energy values." In publishing this principle I did not mention "completely balanced rations," but did use the expression "a ration which is qualitatively complete and quantitatively sufficient"—which has a distinctly different meaning in that the idea of a complete diet provides only for the presence of all required nutrients, in the necessary quantities, while the perfectly balanced ration—literally—must not only be complete, but must not contain an excess of any nutrient. It is true, however, that, at an earlier date, I had—less carefully—used the expression "completely balanced rations" in a similar discussion.[3]

Proceeding further, Mitchell calls attention to my statement that "an individual foodstuff expresses its normal and most characteristic nutritive value—only as it is a part of a ration which is qualitatively com-

[1] SCIENCE, 80: 558–561.
[2] SCIENCE, 77: 306–307.
[3] *Proc. Amer. Soc. Animal Production, Ann. Meeting,* 1932: 32–40.

plete and quantitatively sufficient. . . ." The question which Mitchell raises is, in reality, "which is the 'normal and most characteristic value' of a foodstuff—that determined by its full potentialities, when it is adequately supplemented, or by its limitations, when fed alone?" The difference is simply one of point of view. It is normal to use feeding stuffs as components of approximately complete rations; they are not commonly fed alone; and I have used the word "characteristic" to mean "representative."

Mitchell states that "the recent developments in the net energy conception, initiated and defended by the Pennsylvania group, have tended to complicate the problem of net energy determinations and perhaps even to discourage those who have hoped to put the conception to practical use in the rationing of farm animals."

There have been no recent developments in the net energy conception, so far as I know. It remains as at first proposed, and it is as unassailable as the law of conservation of energy. But there has been much new light cast upon the subject of energy metabolism, and a searching analysis of the problem of determining energy values, in studies published from this institute—which, however, should be discouraging only to those who adhere to the objective of determining net energy values *of individual feeding stuffs as constants.*

The idea of determining net energy values of rations, however, is worthy of consideration. This is a logical deduction from the work of this institute. I have made this deduction; have advocated the determination of such values, and have enumerated some of their apparent uses in the study of problems in the field of animal production.[3]

In regard to Mitchell's speculations as to the cause of specific dynamic action, the relation of the dynamic effects of nutrients to the combinations in which they are fed, etc., we do not care to comment, especially since the methods of determination of specific dynamic effects, and the measurements of these effects—in the literature—have been so unsatisfactory, in fact, so largely fallacious, in the light of findings of this institute during the past six years, especially as set forth in a very recent paper by Kriss, Forbes and Miller,[4] which places the problem of determining specific dynamic effects of nutrients in a new and vastly improved position.

The new point of view and procedure depend upon Rubner's idea[5,6] of a specific dynamic effect of body substance katabolized, from which follows the hypothesis (Forbes, Braman and Kriss,[6]) of a status of minimum heat production of life in which the energy requirement of the animal would be rendered available without waste of heat—that is, without energy expense of utilization; heat increments (dynamic effects) as usually determined at planes of nutrition below energy equilibrium being less than the true energy expense of utilization by the amount of the dynamic effect of body nutrients katabolized (Forbes, Braman and Kriss[7]); heat increments determined above maintenance, with the heat production of maintenance as the base value, therefore representing the true energy expense of nutrient utilization.

We are free to admit, however, that if—as we have concluded—net energy values of individual foodstuffs are not constants, because of the supplementing effects of food combination, in rations, and other conditions affecting the economy of food utilization, then it is conceivable that, for similar reasons, specific dynamic effects of individual nutrients likewise are not constants. We have unpublished results on conditions affecting specific dynamic action, and a second year's experiments on the subject are in progress.

The recent studies of this institute on specific dynamic effects and their determination afford an improved basis of understanding and procedure from which to investigate this question. In this connection I would propose that it would save confusion to limit the term "specific dynamic effect" to signify the dynamic effect of specific kinds of nutriment, and to use the equivalent term "heat increment" to signify other dynamic effects—that is, those which are not specific of particular kinds of nutriment.

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[4] *Jour. Nutrition*, 8: 509–534.
[5] "Die Gesetze des Energieverbrauchs bei der Ernährung," Leipzig und Wien, 1902, S. 370.
[6] *Jour. Agr. Research*, 37: 285, 1928.
[7] *Jour. Agr. Research*, 40: 77, 1930.

MORE EVIDENCE ON THE STRUCTURE OF CHROMATOPHORES

A RECENT communication by Herrick[1] regarding the discussion between Sumner and Mast as to the nature of the chromatophore leads me to enter the lists. Like Herrick, I am not concerned with the problem of terminology; I disagree with Herrick, however, on several points of structure and function. The evidence I wish to present in brief, below, is from two types of chromatophore differing from each other and from Herrick's material. Herrick used epidermal melanophore of frog tadpole; my observations were on melanophore of goldfish and chromatophore of squid.

First, Herrick comments that he has "seen no evidence to support the statement of Mast[2] that pigment granules move on definite paths through the cytoplasm." In melanophores of goldfish with Chambers'

[1] SCIENCE, March 16, 1934.
[2] SCIENCE, November 10, 1933.

micromanipulator,[3] I have been able to push the pigment granules entirely out of place; they slip back into the same position, however, when the needle is removed. Nor is this the result of purely mechanical pressure—it can be seen in living untouched cells, though less strikingly. Likewise, when the pigment granules are so pushed out of place I have been able to see definite intracellular channels, evidenced by differences in the organization of the cytoplasm, in the place where the granules have been.

In the next place, I have observed that, untouched, the rate of movement of these granules varies as the distance from the central pigment mass. Under stimulation with the needle, the rate is definitely correlated with the distance from the point of application of the needle and the state of aggregation of the parent granule mass. I have seen no jerkiness or variableness in rate of movement that could not be explained as necessitated by the position of the granule in the stream. Nor did I ever see one granule lingering and then overtaking others.

On the other hand, however, living squid chromatophores in tissue cultures[4] will often pulsate without changes in the position of the pigment, which may at such a time be highly diffused in clumps, or scattered, leaving absolutely clear and entirely homogeneous unchannelled spaces in the chromatophore. At other times, when the chromatophore pulsates, the pigment occupies not nearly the whole area of the visible sac-like chromatophore. In this material, then, there is no evidence of definite paths in the cytoplasm nor of regular rate of movement of the granules.

To my mind this situation proves to be just another of those cases in which we tend to attempt to bring under one head a number of phenomena which have similar appearance but entirely different structural or functional nature. The work of Parker and his students, and others, seems to indicate that this is true of the control of the chromatophores: my impression is that investigators may well agree that it is also the case as regards their nature and activity.

ELLINOR H. BEHRE
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IS THERE A DIGESTIVE CANAL IN CILIATES?

COSMOVICI[1] recently reported seeing a coiled canal running from the cytostome to the cytopyge in *Colpidium colpoda*. Hall and Alvey[2] failed to confirm this observation. Recently I noticed a peculiar thing which tends to confirm Cosmovici's results.

While feeding carmine to Protozoa I saw an individual of *C. striatum* which had long strings of carmine in its cytoplasm. The appearance could easily have been caused by the animal's having taken carmine into a digestive canal, such as that described by Cosmovici. This individual entirely lacked typical food vacuoles, although others in the preparation were forming them readily. Another specimen from the same culture possessed both carmine strings and food vacuoles. These two were the only individuals seen to have these carmine strings, despite repeated attempts to find others.

Hall and Alvey criticize Cosmovici's interpretation of his results by pointing out that the canal seen by the latter may well have resulted from the conditions of his experiments and thus not be a normal structure. This is in accord with my own view; I can not yet believe that a digestive canal occurs in normal Protozoa. Nevertheless, the limited observations reported here could not easily be explained by the same type of criticism. It would appear, therefore, that the question of a digestive canal in Protozoa is not yet settled.

ARTHUR N. BRAGG
UNIVERSITY OF OKLAHOMA

THE BLUE LIGHT IN THE SEA

IN SCIENCE of November 30, 1934, Dr. Beebe wrote a preliminary statement of the results of his descents into the sea in the bathysphere during the summer of 1934. In the course of his investigations of the undersea illumination he made the following interesting observations:

> The day of the first dive was an exceedingly brilliant one, and the surface of the sea very calm. In consequence, light was still visible to the eye at 1900 feet, 200 feet farther than on any previous dive to this depth. At 2000 feet not the slightest hint of illumination was observable.
>
> A problem of color not yet explained is that from 200 feet down, through the spectroscope, the blue is gradually replaced by violet, until at a depth of 400 feet the latter color is dominant. Yet to the eye, at no time of the descent is there any trace of violet or lavender, only the strongest of blues, appearing brilliant long after it has lost all power for actually seeing anything in the bathysphere.

It seems that the blue fluorescence of the eye when subjected to ultra-violet and violet light may be the explanation of the fact that to Beebe the light appeared a blue color, whereas in the spectroscope only violet light was seen. Professor R. W. Wood in public lectures some years ago demonstrated in a very striking manner the "violet haze," as he called it, which was seen by the eye stimulated with ultra-violet

[3] Reported before the Louisiana Academy of Sciences, Shreveport, La., March, 1932.
[4] Reported before the Louisiana Academy of Sciences, Ruston, La., March, 1933.
[1] C. R. Soc. Biol., Vol. 106, pp. 745–749, 1931.
[2] Trans. Am. Micros. Soc., Vol. 52, pp. 26–32, 1933.

light. In his experiments he used a mercury arc surrounded with black glass, which transmitted mainly the 366 lines of mercury. When this radiation fell into the eye it caused fluorescence of the materials of the eye, with the result that the observer saw a violet haze, which, being in the eye, was not useful for seeing anything. The effect corresponds exactly with the last sentence above quoted from Beebe.

The color of the eye fluorescence is somewhat uncertain. Wood spoke of it as a "violet" haze. W. de Groot[1] arranged an experiment in which various people looked at ultra-violet lines, and presented the results thus: "For 3650, 3345 and 3261 the description which the persons gave of the color was remarkable. They described it as a clear blue whereas the Hg line 4047 and Zn line 4057 were described as violet. It seemed to them as if the succession in the spectrum was reversed. To myself the color appeared more greyish, although with a hue distinctly bluer than that of the recognized 'violet' lines."

It must be remembered that Dr. Beebe was observing the phenomenon on a grander scale than has been produced in the laboratory. The entire scene which he saw through the quartz window of the bathysphere was lighted with the shorter wave-lengths of the daylight spectrum.

To work out the effects quantitatively will require more exact data than are available at present on the absorption coefficients of sea water for visible and near-ultra-violet light and on the visibility curve of the eye extended into the ultra-violet region of the spectrum.

On the basis of the foregoing explanation one is led to wonder about the fluorescence of the eyes of fish. The fluorescence would be troublesome for undersea daylight vision at these depths, and its absence from the eyes of creatures in such an environment would appear to be a favorable adaptation.

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UNUSUAL SKY APPEARANCE

A CORRESPONDENT from Vienna, Va., writes that on either January 22 or 23, about 8 o'clock in the evening, she saw a light flashing in the southwest something like lightning. It would flare up several times, then die down. As she watched it, it became very vivid till it seemed to come from a great blazing light, almost a ball of fire. All this time it was moving around the horizon from the southwest until it had almost reached the starting point. She thought it perhaps more vivid when in the north, and that it seemed to be dying away in the southeast. It appeared to be very low, just showing above the foothills.

I myself was driving along Wisconsin Avenue in Washington on the evening in question, with my wife, and we were startled by what was probably the same appearance. It resembled what is called "heat lightning," only that it seemed to be very near indeed and not associated with any noise. The night, as I recall it, was very cold and dry, and I believe on the turn between two contrasting types of weather.

I would appreciate it if any of your readers will suggest to me an explanation.

C. G. ABBOT

SMITHSONIAN INSTITUTION

BOOKS AND LITERATURE

THE MICROPHYSIOLOGY OF NERVE

The Microphysiology of Nerve. By GENICHI KATO. 139 pp., 1934. The Maruzen Company, Ltd., Tokyo, Japan.

IN this concisely written monograph, Professor Kato has presented the results of a series of experiments utilizing his technique for isolating single nerve or muscle fibers in the Japanese toad. Using preparations in which either a single nerve or muscle fiber or both have been dissected free, Kato and his co-workers have abundantly demonstrated that the nerve impulse completely recovers after passing through a narcotized region. The magnitude of the conducted response of a single muscle fiber stimulated through a single nerve fiber is always the same at any strength of stimulus above threshold. Graded, non-conducted muscle fiber contractions localized at the site of small stimulating electrodes are obtainable only with weak stimuli and are unaccompanied by action potentials. Kato compares these responses to peculiar localized contractions occurring as a result of stimulation of a completely narcotized region of a muscle. Both of these types of contraction are found only under restricted conditions as a result of artificial stimuli and are entirely different from the conducted contractions in which there is no deviation from the all-or-none principle.

In observing spinal reflexes, Kato has shown that ipsilateral afferent stimuli are inhibitory to a crossed-extensor reflex (frog) at certain moderate current strengths, while with greatly increased strength of stimulation of the same nerve trunk the effect is summation with the crossed stimulation. This summation is a function of fibers which originate from free nerve endings in the epidermis, whereas the inhibitory effects

[1] *Nature*, September 29, 1934.

result from stimulation of nerves arising in muscles. He suggests that there are two types of afferent nerve fibers: (a) inhibitory fibers, easily narcotized and having a low threshold of stimulation and (b) excitatory fibers which are less susceptible to narcotization and have a high threshold. Kato has isolated these two types of fibers and has demonstrated that the central effect of the inhibitory fibers, which are about 9.5μ in diameter, is only inhibition with stimuli of any strength or frequency even after the application of strychnine. Stimulation of the excitatory afferent fibers, whose diameter is 6 to 7μ, results only in summation with crossed excitation. Kato has also localized an inhibitory center at the level of the *lamina terminalis* from which fibers are projected into the cord decussating slightly caudal to the crossing of the motor tract.

Kato does not offer experiments that would refute the view, now generally prevalent, that the nerve impulses which give rise to inhibition do not differ fundamentally from those whose central effect is excitatory. Evidence is accumulating from many sources tending to show that not only are impulses in nerve fibers non-specific but also in intra-central terminals as well. Therefore, whether a discharge into the cord gives rise to excitation or inhibition depends upon the nature of the reactions set up at the particular point on the neurone at which the discharging nerve terminal forms a synapse. The significance of Kato's experiments lies in the fact that they lend support to the hypothesis that a particular synapse when discharged by its nerve fiber always produces the same non-reversible effect; one synapse when activated always develops excitatory state, and another always inhibitory state. However, a single afferent fiber may end not only in nerve terminals (boutons terminaux) which contribute to the development of an excitatory state in one neurone, but it may also send collateral branches to another nerve cell or cells on the same side of the cord, which end in boutons whose discharge results in inhibition.

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THE GRASSES OF THE UNITED STATES

Manual of the Grasses of the United States. By A. S. HITCHCOCK. U. S. Dept. Agr. Miscel. Publ. 200: 1–1044. figs. 1–1696. 1935. Superintendent of Documents, Government Printing Office, Washington, D. C., $1.75.

No family of plants is of such outstandingly great importance to man as is the grass family, including as it does all our cultivated cereals, the basic foods of the majority of mankind, most of the wild and cultivated species on which the grazing and dairy industries are based, and numerous species otherwise of great economic importance. It is thus fitting that the first comprehensive treatment of the entire family, as represented in the continental United States, should appear under government auspices. It is a botanical contribution of first magnitude and one of great economic and scientific moment. In the introductory pages the uses, distribution, morphology, classification and nomenclature of grasses are considered, followed by a key to the tribes and genera, while under each genus is a key to the species. There are 159 numbered genera and 1,100 numbered species, with additional data appertaining to casually introduced and cultivated forms. Each species is illustrated, while the accompanying maps graphically indicate the geographic distribution in each case. The descriptive text is not encumbered with synonyms, but for those who must consider synonymy, a full list of synonyms, by accepted species in alphabetic sequence, is given at the end of the work, pages 771–982. Here and there in the synonymy critical notes are given and for all originally published species, as contrasted to transfers, the type locality is indicated. How complex synonymy has become may be evidenced from the fact that for a number of species more than 20 synonyms are listed, and for at least one species more than 70 synonyms are given. This list of synonyms provides the basis of selection of the accepted name in each case, the nomenclature following the International Rules. The compilation of this list, a major task, shows evidence of most careful and critical bibliographic and herbarium work, and there seems little chance that few if any "earlier" names will be detected by future workers that would replace those accepted in this important work.

The work is planned to meet the needs of the botanist, the agronomist, the forester and the agriculturist, hence the inclusion of supplementary economic notes under the various genera. Common names of cultivated species follow "Standardized Plant Names," while those for native and naturalized species have apparently been arbitrarily selected, as were many of those in that work; for these the author is not responsible (p. 14). Thus under *Muhlenbergia* one notes the most unusual and apparently new common name "muhly," while fox tail, which is widely used for *Setaria*, is replaced by bristle grass and the name for fox tail is associated with *Alopecurus*. These arbitrary changes can not conceivably effect accepted usage, and unquestionably it would have been better to apply common names, as does the man on the land, rather than to have invoked arbitrary selection.

This is a major contribution to our knowledge of the grasses of North America, marks the culmination of more than thirty years of intensive work on the part of the author, and will be found to be of great

value not only to botanists in diverse fields, but to a great number of individuals interested in various phases of agriculture, forestry, conservation, soil erosion, irrigation and other fields. Fortunately for those who need and must have this work, it is a public document and is so priced as to be available to all.

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SOCIETIES AND MEETINGS

THE INDIANA ACADEMY OF SCIENCE

THE golden anniversary meeting of the Indiana Academy of Science was held on Thursday, Friday and Saturday, November 15, 16 and 17 at Indianapolis, with the academy as the guest of Butler University. The general meetings were devoted to its history and the honoring of its living founders. At the sectional meetings a total of ninety-eight papers on botany, chemistry, bacteriology, geology, geography, physics, mathematics and zoology were read. The meetings were all well attended.

The principal address of the historical meeting was given by Dr. Will E. Edington, of DePauw University, on "There Were Giants in Those Days." The address dealt with the various factors that led up to the founding of the academy in 1885, and was illustrated with slides showing the principal founders. Among these were David Starr Jordan, T. C. Mendenhall, John M. Coulter, John C. Branner, Daniel Kirkwood, John Sterling Kingsley, Thomas Gray, Oliver P. Jenkins, Richard Owen, Alexander Smith, Harvey W. Wiley, Joseph Swain, William A. Noyes, Amos W. Butler, Barton W. Evermann, Lillien J. Martin, Carl H. Eigenmann, Willis S. Blatchley, Joseph C. Arthur, Stanley Coulter and others. Following this address ten of the fifteen living founders who were present were introduced to the assembled members of the academy.

The president's address was delivered by Father Julius A. Nieuwland, of the University of Notre Dame, on "The Story of Synthetic Rubber," which was a report on the work for which he has been awarded the Nichols Medal by the American Chemical Society.

The Founders' Dinner was held on the evening of November 16, at the Claypool Hotel with several hundred members in attendance. Following the dinner, the ten living founders who were present gave short talks. These founders are J. C. Arthur, George W. Benton, W. S. Blatchley, J. B. Burris, Amos W. Butler, Stanley Coulter, Robert Hessler, David M. Mottier, William A. Noyes and A. J. Phinney. They were presented with certificates of appreciation for their service to science and to the academy, John S. Wright, of the Eli Lilly Company, acting as master of this ceremony.

Several scientific men from without the state were present. Of these particular mention may be made of Dr. Henry B. Ward, permanent secretary of the American Association for the Advancement of Science. Dr. Ward attended the meetings of the executive committee and made a short address at the founders' dinner in which he discussed the meeting of the association to be held in Indianapolis in 1937.

The Junior Academy, composed of a number of high-school science clubs, held its meetings on Saturday morning. These included scientific exhibits.

There were on display a number of scientific exhibits and also an exhibit of photographs of all the past presidents of the academy and a majority of the founders. It is the intention of the academy to file these photographs, slides made from them and other historical material in the State Library, so that it will be accessible for use in lectures and other work. At the request of Dr. Ward photographs of all the past presidents are to be exhibited at the St. Louis meeting of the American Association for the Advancement of Science.

The following officers were chosen for 1935: *President,* Will Scott, Indiana University; *Vice-President,* Will E. Edington, DePauw University; *Secretary,* Ray C. Friesner, Butler University; *Treasurer,* William P. Morgan, Indiana Central College; *Editor of the Proceedings,* Paul Weatherwax, Indiana University; *Press Secretary,* Thomas R. Johnston, Purdue University. The next winter meeting will be held at Crawfordsville, Indiana, with Wabash College as host.

WILL E. EDINGTON

SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE NICOTINE VAPORIZER, A DEVICE FOR UTILIZING NICOTINE IN THE CONTROL OF INSECT PESTS

FOR many years nicotine has been available in commerce in the form of nicotine sulfate having a content of 40 per cent. nicotine alkaloid. In the control of insect pests attacking vegetation under outdoor conditions, this material has been utilized in two ways, as an aqueous spray solution and as a dust mixture. The insecticidal action appears to be due very largely

to the volatilization of the nicotine. In order to produce a more rapid liberation of the nicotine, various "activator" substances, such as hydrated lime, lime-sulfur, an ammonium sulfate, have been added to the spray and dust. Attempts have also been made to increase the effectiveness of nicotine dust by discharging into the blast of dust the exhaust of the gasoline engine operating the blower, the slightly higher temperature tending to liberate the absorbed nicotine and produce a greater degree of volatilization.

Various insects attacking plants in greenhouses have been controlled by the vapor of nicotine produced by burning tobacco stems or a material on which nicotine has been placed, and by placing nicotine on a heated object.

The new device, which we have designated a nicotine vaporizer, has been designed with the object of effecting the control of insect pests of orchard, garden and field crops by means of nicotine sulfate or any form of nicotine concentrate applied as a vapor produced by heat or as a vapor-like mist produced by atomization. The essential features of the device provide for atomizing the nicotine, conveying the mist through a heated chamber where it is vaporized with the formation of dense fumes, and thence conveying the vapor through a blower to the vegetation; or the finely atomized nicotine may be conveyed through the blower to the vegetation without being vaporized.

The machine which we have built and tested operates in the manner described as follows: The nicotine is contained in two chambers connected through a pressure regulator to a compressed air tank. Tubes arranged to produce atomization lead from the chambers and discharge into two copper pipes 2 inches in diameter and 30 inches in length. The pipes are inclosed in a shield to conserve heat. They are heated to a temperature of approximately 350° C. by a gas burner, utilizing compressed gas, extending lengthwise below them. The pipes extend into the intake of the blower of a standard type of duster used in insect control work. The blast of air from the blower carries the nicotine vapor or the atomized nicotine to the vegetation. The rate with which the nicotine is fed through the atomizer is governed by the pressure regulator.

Tests made with the vaporizer in the control of the codling moth, *Carpocapsa pomonella* Linn., have indicated that nicotine applied as a vapor is far more potent as an insecticide than where applied in the usual form of a spray or a dust. It is a well-known fact that nicotine has no appreciable effect on the codling moth where applied as a dust, or as a spray at the usual concentration of one pint of nicotine sulfate to 100 gallons of water. An apple tree having a volume of approximately 4,000 cubic feet requires about 20 gallons of spray in order to effect a thorough coverage. With this quantity of spray the tree receives 90 cubic centimeters of nicotine sulfate. Tests have shown that 10 cubic centimeters of nicotine sulfate properly applied with the vaporizer will kill all the moths in a tree of this size.

The effectiveness of the treatment depends upon the concentration of the vapor in the atmosphere surrounding the insect and upon the length of time the insect is subjected to the vapor. The maximum degree of effectiveness is secured by discharging the vapor under a canvas cover dragged over the crop to be treated. For the treatment of orchard trees we have built and tested, with a fair degree of satisfaction, a device by means of which large trees may be inclosed and treated at the rate of one tree each half minute. This device consists of a transverse boom extending over two rows of trees, supporting a large canvas cover, adjustable for trees of different sizes, and provided with two curtains which permit inclosing the trees quickly and completely, all mounted on an automobile truck.

The development reported in this article owes its origin to a suggestion to try burning nicotine, made by the junior author, Mr. Persing, in connection with tests on fumigating with hydrocyanic acid to control the codling moth.

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PRODUCING BRAIN LESIONS IN RATS WITHOUT OPENING THE SKULL

HERETOFORE all localized brain lesions in experimental animals have been produced by opening the skull and introducing some destructive agent, usually a knife or a thermocautery. Using heat as the destroying agent, we have found it possible to shorten and simplify the older procedure considerably by applying the cautery point *extracranially*. If a knife is used, it is of course necessary to trepine the skull. Heat, however, will readily penetrate the unremoved bony shell sufficiently to coagulate the underlying tissues. This technique is especially feasible when the skull bones are thin, as in the rat.

On some occasions, there may be good reasons for the use of a cutting edge and hence for removal of a portion of the skull. Even when tissue is destroyed by heat, there may be occasions when the heat should

be applied directly. Nevertheless, we are of the opinion that the current practice of trepining before thermocautery is a neurological tradition rather than an ideal procedure. In a species with poorly marked cortical surfaces, it can not be of much aid to have the surface in view at the moment of operation. The maps of lesions presented by current investigators do not indicate that the prevailing techniques consistently produce the desired destruction. In consequence of this lack of control of cerebral lesions, the researcher produces lesions in many animals and selects for study the animals which happen to possess the sort of destruction which he wishes to study, disregarding the remainder.

This general procedure must be followed today, regardless of how the lesions are produced. If a hot instrument is applied extracranially, the production of lesions is an extremely easy process. The rat is anesthetized, the skull exposed, the cautery applied (in our instance, for fifty seconds), the wound sewed and covered with collodion. Aside from preliminary anesthetization, the entire operation can be performed in three minutes. The skull is left intact. Far from being a cruder method, this method seems to us to provide as good or even better control of the lesion than does the more complicated technique.

The technique has been entirely successful in meeting our needs. We wished to destroy all or most of the striate area. By examining the relation between the striate area and the skull markings, we determined where the cautery should be applied. Experimentation upon rats other than the main experimental group showed what duration of exposure to the heat would most often produce the desired destruction. Examination of sections, to be reported in detail later, show that the desired effect with respect to location, depth and shape of lesion was produced more often than reports of other investigators would lead one to expect from the employment of the traditional methods.

Our lesions were in general round in shape, two millimeters in diameter and were limited to the cortex. It seems likely, however, that one could devise cautery points which would produce lesions of almost any desired shape, and that these lesions could be produced at any point adjacent to the skull. The depth of the lesion may be controlled by varying the duration of the application of the heat, or by varying the intensity of the heat. It is even possible that almost complete decortication might be produced by applying a relatively small cautery point to many areas or by making a metal cap to fit the skull and then applying it when heated.

In addition to simplicity, the technique has the advantage of completely avoiding exposure of the cranial contents to the danger of infection.

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SPECIAL ARTICLES

A FILTERABLE VIRUS RECOVERED FROM WHITE MICE

DURING recent work with the viruses of equine encephalomyelitis and hog cholera an infective agent was obtained from white mice which was pathologically and serologically distinct from both viruses. Its origin was not definitely known, but it seemed likely that the natural host of the agent was the mouse, in spite of the fact that in our mouse colony no disease had been previously recognized. In an experiment designed to trace the origin of the infectious agent, 60 five-week-old, healthy-looking mice from our colony were each given an intracerebral injection of a small amount of sterile bouillon. Fifty-one of these mice showed no evidence of illness during the three weeks that they were under observation. Four died in from 3 to 13 days following the inoculation, and three were killed on from the sixth to the eighth day when they showed symptoms similar to those observed in the mice inoculated with the unknown agent. On the sixth day two additional mice that showed photophobia but no other symptoms were killed. From one of these mice no material was obtained for inoculation, but bacteriologically sterile suspensions of the brain of each of the other eight when injected into guinea-pigs caused symptoms which could not be differentiated from those produced by the original material. This experiment, together with others, suggests that the infectious agent is carried by apparently healthy mice in our colony and that symptoms may be brought out by the intracerebral injection of foreign protein.

Among the mice from our colony only about 60 per cent. develop symptoms after intracerebral injection of infectious material and only 40 per cent. die. The incubation period is from 5 to 10 days. The clinical symptoms are somnolence, photophobia, tremors of the legs, followed by tonic spasms of the muscles of the hind quarters, shown when the mouse is lifted by its tail. Paralysis has not been observed. One of 30 mice inoculated with infectious material by the intraperitoneal route developed symptoms, while

intravenous and intracutaneous inoculations into the footpads have been negative. The agent has been demonstrated in the brain as well as in the viscera of mice that have succumbed to the infection. Macroscopically the only changes noted are a nutmeg liver and slight enlargement of the spleen. A preliminary microscopic examination shows a certain degree of infiltration of the meninges, ependyma, choroid plexus and perivascular lymph spaces with round cells. In addition there is necrosis of some of the nerve cells in the cerebral cortex, cerebellum, brain stem and spinal cord. In the last the anterior horn cells are predominantly involved. In the cerebellum it is the Purkinje cells that are affected. There may be some proliferation of the ependyma and of the glia cells of the gray matter.

Guinea-pigs have proved to be very susceptible as they develop symptoms following intracerebral, subcutaneous and intranasal inoculation. The mortality has varied with different strains used but has been practically 100 per cent. after intracerebral inoculation and from 80 to 90 per cent. following subcutaneous injection. The course of the disease is more chronic than in mice, there being a remittent type of fever with emaciation, somnolence, salivation and markedly labored breathing. Death occurred in from 10 days to 3 weeks after inoculation. One of eight guinea-pigs in contact with an infected animal developed the disease. At autopsy pneumonia of the virus type is often encountered. In addition to the changes noted in the mouse brains, acidophilic intranuclear inclusions have been found in the round cells present in the meninges and choroid plexi. The infectious agent has been demonstrated in the brain, blood and suspensions of the diseased lungs. Three guinea-pigs have recovered from the disease and have resisted further injections. In a limited number of experiments attempts to infect rabbits have been negative.

Material known to be infectious has shown no organized forms when examined by the usual bacteriological procedures and no growth has occurred on a variety of media. The disease has been produced by material passed through Berkefeld "N" and "W" filters that have held back *B. prodigiosus,* and also by material that has been in 50 per cent. glycerol for at least one month. From these facts we conclude that the agent is a filterable virus.

The disease caused by this virus is definitely different from infectious ectromelia.[1] The virus of spontaneous encephalitis of mice described by Theiler[2] produces a different clinical picture and is confined to the central nervous system, whereas the virus we have been working with is distributed generally. The origin of the virus recovered by Armstrong[3] from a monkey inoculated with virus from a human case of encephalitis during the St. Louis epidemic has not been definitely established. It produces a clinical picture in mice which is strikingly like that described above, and the lesions in the central nervous system have much in common with those observed in our animals.

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THE RELATION OF STREAM DOUBLE REFRACTION TO TOBACCO MOSAIC VIRUS

IN a previous publication[1] we reported that juice expressed from tomato tissues infected with tobacco mosaic virus contains a high concentration of M.C.S.D.R. (material causing stream double refraction), whereas juice from healthy tissues contains a relatively slight concentration of material causing this phenomenon.

The high concentration of M.C.S.D.R. in mosaic plants is probably subject to one of the following three explanations. (1) The M.C.S.D.R. in mosaic plants may be the same material as that in healthy plants, but is in much higher concentration in mosaic plants. (2) The stream double refraction exhibited by juice from mosaic plants may be caused by a high concentration of virus particles, together with a very low concentration of the material which causes stream double refraction in healthy plants. (3) Most of the M.C.S.D.R. in mosaic plants may be composed of a product of the virus or of the diseased host not present in healthy plants.

Previous work[2] has shown that Vinson's purification technique removes all the detectable M.C.S.D.R. from juice of healthy plants but leaves a high concentration of M.C.S.D.R. and virus in infective juice. When different methods of juice extraction were used it was found[1] that the method which yielded the highest concentration of M.C.S.D.R. from mosaic plants yielded the lowest concentration from healthy plants and the method yielding the highest concentration from healthy plants yielded the lowest from mosaic plants. When juice from healthy plants has been stored at room temperature for from 12 to 24 hours it no longer exhibits stream double refraction, whereas juice from mosaic plants contains a concentration of M.C.S.D.R. even slightly higher than freshly extracted

[1] J. Marchal, *Jour. Path. and Bact.*, 33: 713, 1930.
[2] M. Theiler, SCIENCE, 80: 122, 1934.
[3] C. Armstrong, with pathology by R. D. Lillie, *Publ. Health Rep.*, 49: 1019, 1934.
[1] W. N. Takahashi and T. E. Rawlins, "Application of Stream Double Refraction in Identification of Streak Diseases of Tomato." *Phytopath.* In press.
[2] W. N. Takahashi and T. E. Rawlins, SCIENCE, 77: 284, 1933.

juice. All the above results indicate that the M.C.S.D.R. in healthy plants and that in mosaic plants have different properties and suggest that they may be different substances. This evidence therefore favors the second or third explanations given in the preceding paragraph.

If most of the stream double refraction produced by juice from mosaic plants is due to tobacco mosaic virus particles one should find the concentration of virus and M.C.S.D.R. to be positively correlated. In order to gain evidence on this relation juice was extracted from tissues which differed greatly in virus content. Different organs of mosaic tobacco plants, leaves of different hosts and chlorotic and dark green tissues of mosaic tobacco leaves were used as virus sources.

The critical dilution, which is the minimum amount of dilution required to cause the disappearance of stream double refraction, was used as a measure of the concentration of M.C.S.D.R. in infective juice. The virus concentration was determined by a modification of the half leaf method of Samuel and Bald.[3]

Following are typical examples of the critical dilutions found for infective juice from various tissues: Tobacco leaves, 1:768; tobacco roots, 1:256; tobacco stems, 1:96; tomato leaves, 1:256; *Martynia louisiana* leaves, 1:256; *Nicandra Physalodes* leaves, 1:224; chlorotic tissues of mosaic tobacco leaves, 1:2048; dark green tissues of mosaic tobacco leaves, 1:256. When the virus concentration in each of the above critical dilutions was determined by the half leaf method all were found to be approximately the same. (Differed by less than 12 per cent.). This work has been repeated a number of times with similar results. It is therefore evident that when samples of juice obtained from different sources and containing different concentrations of virus are diluted until the stream double refraction just disappears all the diluted samples contain approximately the same concentration of virus. The stream double refraction technique therefore provides a rapid and satisfactory method for determining virus concentration in fresh juice or that which has been preserved by freezing, the virus concentration the original undiluted sample being proportional to the dilution required to cause the disappearance of stream double refraction.

Heating mosaic juice to 100° C. for 10 minutes is known to inactivate tobacco mosaic virus and was also found to destroy the power of the M.C.S.D.R. to produce stream double refraction. A heavy precipitate was formed during the heating, and it is supposed that the M.C.S.D.R. was coagulated and was therefore unable to cause stream double refraction.

[3] G. Samuel and J. G. Bald, *Ann. Appl. Biol.*, 20: 70–90, 1933.

If the virus particles are not the colloidal particles causing most of the stream double refraction exhibited by juice from mosaic plants they may have a different size or a different isoelectric point and if so the virus should be separable from the M.C.S.D.R. by ultrafiltrations or electrophoresis. All experiments conducted have indicated that the M.C.S.D.R. in the mosaic plants behaves the same as the virus during ultrafiltration and electrophoresis and can not be separated from the virus by such treatments. All the above evidence has favored the hypothesis that the virus particles are responsible for most or all of the stream double refraction exhibited by juice from mosaic plants.

Two conditions were found in which virus concentration was not positively correlated with concentration of M.C.S.D.R. In certain samples of aged virus from mosaic tobacco plants the concentration of active virus was found to be much lower than that of M.C.S.D.R.; and in virus treated with ultrasonic radiation the virus was completely inactivated after two hours,[4] whereas the concentration of M.C.S.D.R. remained high. These two experimental results are probably subject to one of two interpretations: (1) That the virus and M.C.S.D.R. are different; (2) that the virus particles inactivated by aging or ultrasonic radiation are not changed in external form sufficiently to prevent stream double refraction.

Although much of the evidence cited above favors the supposition that the virus particles are the causal agent of most of the stream double refraction exhibited by juice from mosaic plants the evidence remains inconclusive. However, since the concentrations of virus and M.C.S.D.R. in fresh juice or that preserved by freezing have always been found to be positively correlated the stream double refraction technique provides a rapid and reliable method for determining virus concentration in such juice.

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